REMARKS

In an Office Action dated April 17, 2008, claims 1-8, 11, 13-19, 22-36, 38-40, 53-61, 133-136, and 173-177, all of the claims then under consideration in the above-referenced U.S. patent application, were rejected. In view of the above amendments, the following remarks, and the accompanying documents, Applicants respectfully request reconsideration of this application, and allowance of the claims, as amended.

Claims 1, 5-8, 11, 23, 25-28, 33-36, 38-40, 133-136, 173, 175, and 177 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. These rejections are respectfully traversed.

In the Office Action, it is stated that the claims recite the term "conservative variants" and "that conservative variants as defined on page 11 lines 1-6 includes examples of *specific replacements* and the like." (italics added). The Office Action also states that "and the like must be interpreted very broadly". Accordingly, the claims have been amended to recite the specific replacements identified in the Office Action as being at page 11, lines 1-6 of the specification.

The Office Action also states that "the claims do not limit the conservative variants to specific polypeptides recited in the specification". Accordingly, the claims have been further amended to identify specific polypeptides recited in the specification.

In view of the above amendments and remarks, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, based on the written description requirement, is respectfully requested.

Claims 1-8, 11, 23-36, 38-40,133-136, 173, 175, and 177 were rejected under 35 U.S.C. §112, first paragraph, on grounds of lack of enablement. These rejections are respectfully traversed.

In the Office Action it is stated that the claims recite "conservative variants", that the "conservative variants are not limited to a specific number of variations", and that "conservative variants as defined on page 11 lines 1-6 include examples of *specific replacements* and the like." (italics added). Accordingly, the claims have been amended to recite the specific replacements identified in the Office Action as being on page 11, lines 1-6 of the specification. In view thereof, it is submitted that the present claims are enabled.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, on grounds of lack of enablement, is respectfully requested.

Claims 1-3, 5-7, 11, 13-14, 16-18, 22-29, 33-36, 38-39, 53-55, 57-59, 61,133-135 and 177 were rejected under 35 U.S.C. §102(e) as being anticipated by Mann U.S. Patent No. 6,030,948. Claims 4, 8, 15, 19, 30-32, 40, 56, 60 and 136 were rejected under 35 U.S.C. §103(a) as being unpatentable over Mann, Siebert et al. U.S. Patent No. 5,591,716, Luedders et al. U.S. Patent No. 4,261,982, and Rahim et al. U.S. Patent No. 4,863,906. Claims 173-176 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Mann U.S. Patent No. 6,030,948 and further in view of Mann U.S. Patent No. 6,030,948. These rejections are respectfully traversed.

Submitted herewith is a Declaration of Dr. Jo-David Fine, a professor of medicine and recognized expert in the field of Dermatology.

As stated in Dr. Fine's Declaration, he has been informed that it is the position of the U.S. Patent and Trademark Office in an Office Action dated April 17, 2008, that Mann teaches a method of applying a composition containing thymosin β4 "to the scalp (claim 8). Prior to application to the scalp, an acid peel (i.e., chemical peel) solution is applied to the scalp and then removed. The removal of the acid peel solution results in the removal of an outer later of skin and results in ***abrasions/damage/lesions/wounds*** upon the skin." (emphasis added).

As stated in Dr. Fine's Declaration, he has studied U.S. Patent No. 6,030,948 to Mann. For the following reasons, the statement that the acid peel of Mann results in "abrasions/damage/lesions/wounds" on the skin is incorrect, according to the expert, Dr. Fine.

As stated in Dr. Fine's Declaration, column 10, lines 56-62 of the Mann patent states as follows:

> *"In the method of this invention, the following steps are performed in the order noted: (1) cleansing the scalp with a cleansing agent; (2) treating the cleansed scalp with a keratin solvent system; (3) applying a topical anesthetic (optional); (4) applying an acid peel solution; (5) applying a hyperactive urea gel formula (optional) and (6) applying a hair regeneration composition."*

As stated in Dr. Fine's Declaration, acid peel systems are described in Step 4 of Mann, column 13, line 19 to column 14, line 11, and in claims 17 and 18 of Mann, as follows:

> *"Step 4: Acid Peel Systems*
>
> *Application of the optional fragrance-based topical anesthetic is followed by the application of an acid-based system with the composition shown in Table 6. This composition included a series of physiological acids, including citric acid and pyruvic acid, in combination with a surfactant that will enhance penetration and a solubilizing system which also facilitates penetration. The acid peel system is allowed to remain on the scalp for anywhere between 1 minute to 8 hours or more. If the acid peel system is allowed to remain on the scalp for more than about 30 minutes, an occlusive cap may be placed on the head covering the scalp. As used herein, an occlusive cap means any structure, which when placed on the scalp of the head, prevents the acid peel system from leaving the surface of the scalp.*
>
> *The following Table 10 provides a range of concentrations of ingredients that may be used in the acid peel solution.*
>
> *TABLE 10 ACID PEEL*
>
> *Citric acid 20.00 Salicylic acid 10.00 Methyl salicylate 10.00 Menthol 1.00 POLYSORBATE-80 3.00 2-Phenoxyethanol 6.00 Pyruvic acid 10.00 TERGITOL 15-S-7 1.00 Methyl nicotinate 0.50 Alcohol SD40 A (190) 23.00 Demineralized water 15.50*
>
> *The above ingredients are shown in weight percent, and are available from commercial suppliers such as Brooks, Sigma (St. Louis, Mo.) and Aldrich (Milwaukee, Wis.)."*

As stated in Dr. Fine's Declaration, claims 17 and 18 of Mann read as follows:

> *"17. The method of claim 8 wherein the acid peel solution comprises at least one physiological acid.*
>
> *18. The method of claim 17 wherein the physiological acid is citric acid, ascorbic acid or pyruvic acid."*

As stated in Dr. Fine's Declaration, acid peels are used for the purpose of skin exfoliation. The primary use of acid peels is to help rid skin surface areas of dead cells and to stimulate cellular proliferation of a new healthy-looking, smoother, more evenly pigmented,

and “glowing” skin. Mann's patent describes the use of physiological acids (specific acid peels) to increase skin permeability.

As stated in Dr. Fine’s Declaration, claim 17 of the above referenced Mann patent indicates that the acid peel solution comprises at least one physiological acid. Claim 18 indicates that the physiological acid is citric acid, ascorbic acid, or pyruvic acid. Citric acid (a fruit acid), and ascorbic acid (capable of being extracted from fruits), are alpha hydroxyacids (AHAs). Pyruvic acid is an alpha-keto acid. These physiological acids described in the claims are weak acids as are other naturally-occurring AHAs. AHAs are the mildest of the acid or chemical peels and are most widely used for skin exfoliation because of their effectiveness and the absence of toxicity. Other types of acid peels are the Beta-lift peels or the beta hydroxyacids (BHA). BHAs are effective in lifting the topmost layer of skin by "dissolving" the desmosomes which bind it to the underlying epidermis, triggering cell division (proliferation), skin cell production and shedding. An example of a beta hydroxyacid used as an acid peel is salicylic acid. Salicylic acid, which is soluble in oil, can exfoliate oily skin more effectively than other acid peels. At times AHAs and BHAs are used in combination as exfoliants.

As stated in Dr. Fine’s Declaration, the physiologic acids or acid peels identified in the Mann passages quoted above, and claims 17 and 18 of Mann, act by accelerating the shedding or loosening of the topmost layers of the skin (stratum corneum or keratinized epithelium) by decreasing their cohesiveness. The most effective of the AHA peels is glycolic acid.

As stated in Dr. Fine’s Declaration, any person skilled in this art would recognize that surface acting acid peels as disclosed in Mann do not cause “abrasion/damage/lesions/wounds” on skin, as stated in the April 17, 2008 Office Action. As stated in Dr. Fine’s Declaration, one cannot hurt dead cells. As stated in Dr. Fine’s Declaration, the acid peels that Mann describes affect the outermost portion of the epidermis or skin, which is made up primarily of about 15-20 layers of dead cells that lack nuclei. Acid peels do cause surface exfoliation by reducing cellular cohesiveness and/or by denaturing or fragmenting the cell adhesion proteins of the desmosome complex. As stated in Dr. Fine’s Declaration, the acid peel solution that Mann describes, as stated in the patent, increases the

permeability of the skin to his hair regeneration composition, but in no way causes abrasion, damage, lesions and/or wounds on the skin.

As to the obviousness rejections, the Siebert et al., Luedders et al. and Rahim et al. references do not remedy the deficiencies of the Mann reference.

In view of the above Remarks and the accompanying Declaration, withdrawal of the rejections under 35 U.S.C. §102 and §103 based on Mann, alone or combined, is respectfully requested.

Claim 177 was rejected under 35 U.S.C. § 102(b) as being anticipated by Goldstein et al. (U.S. 5,578,570). In view of the above amendments, this rejection is respectfully traversed.

In the Office Action, it is noted that claim 177 was drawn to a method of "prevention", that any patient population is available for preventive administration, and that the patient population described in Goldstein meets the patient population of claim 177.

Claim 177 has been cancelled, and claims 185 and 186 are being substituted therefore.

In claim 185, the term "preventing" has been removed, obviating the rejection based on Goldstein in the Office Action.

Claim 186 is directed to a method of treatment for treating or preventing tissue injury associated with a wound healing disorder, a skin wound, an ulcer, a diabetic ulcer, a venus ulcer, a chronic ulcer, a burn, a muscular-skeletal disorder, arthritis, osteoporosis, neurological or nerve disease, neuron-degenerative disease, cardiovascular disease, ischemia, atherosclerosis, a tissue wound, tissue damage due to ischemia, ischemic brain disease, ischemic bone disease, ischemic heart disease, corneal tissue damage of the eye, retinal tissue damage of the eye, inflammation, epithelial tissue damage, tissue damage due to surgical procedures, tissue damage due to irradiation, tissue damage due to laceration, tissue damage due to toxic chemicals, tissue damage due to viral infections, fibrotic disorder, sclerotic disorder, a disorder associated with under-expression of Tβ4 or a Tβ4 isoform, a recurrent wound, a tissue repair disorder, a fibrotic tissue disorder, an eye related wound, a deficiency in endometrial growth, endometrial tissue damage, a deficiency in placental growth, inability to maintain pregnancy, or a deficiency in endometrial-trophoblast interaction, in a subject in need of such treatment.

Goldstein relates to a method of inhibiting the progression of septic shock in a subject. Applicants submit that Goldstein discloses administering thymosin B4 to a mammal in which a

sepsis cascade is occurring. Thus, Goldstein teaches administering thymosin B4 to a subject suffering from septic shock to inhibit the progression of the sepsis cascade. There is no mention of treating or prevention of tissue injury in Goldstein.

Goldstein in no way discloses or renders obvious preventing tissue injury associated with the indications set forth in claim 186, in a subject in need of such treatment.

In view of the above amendments and remarks, withdrawal of the rejection under 35 U.S.C. § 102(b) based on Goldstein et al. is respectfully requested.

The Office Action contains several obviousness-type double patenting rejections. In regard to the double-patenting rejections based on serial no. 10/714,405, such application is not commonly owned. However, serial no. 10/714,405 has been abandoned as of July 16, 2008, by not filing a response to an Office Action. No continuation or divisional application has been filed.

As to serial no. 10/853,505, an appropriate Terminal Disclaimer is being submitted herewith in respect of such application, along with a terminal disclaimer in respect of commonly owned serial no. 11/284,430.

As to serial no. 11/284,408, such application is not commonly owned. Serial no. 11/284,408 was filed to copy claims of U.S. Publication No. 2003/0228266 and U.S. Patent No. 6,821,524, for a possible interference. The present application may be prior art to at least some of the claims of serial no. 11/284,408, and patentability of any such claims will have to be established over the present disclosure.

As to serial no. 11/917,869, such application is not commonly owned. Claims 13-23 and 26 of serial no. 11/917,869 are directed to a method of treatment for treating, preventing, inhibiting or reducing tissue deterioration, injury or damage resulting from administration of a quaternary ammonium salt to a subject.

The present application is prior art to serial no. 11/917,869. Accordingly, the patentability of claims 13-23 and 26 of serial no. 11/917,869 will have to be established over the disclosure of the present application.

In view of the above amendments and remarks, and the accompanying documents, withdrawal of the double-patenting rejections is respectfully requested.

Applicant submits that the present application is now in condition for allowance. Reconsideration and favorable action are earnestly requested.

Respectfully submitted,

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